Journal of
Research in Pharmacy

Research Article

www.jrespharm.com

Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions

Abhishek KANUGO [1]*, Yash GANDHI[1]

[1] Department of Pharmaceutics, SVKM NMIMS School of Pharmacy and Technology Management, Shirpur, Dhule, India-425405.

*Corresponding author: E-mail: abhi.kanugo09@gmail.com, M: 09284513359.

Received: 3 March 2022 / Revised: 27 April 2022 / Accepted: 7 May 2022

ABSTRACT: Allergic rhinitis or allergic conditions are associated with the symptoms such as running nose, frequent headache, sore throat, watering of eye, and sometimes coughing as well as eczema also. The delay in the treatment or ignorance may leads to severe health problems like asthma, inability to sleep, severe redness, etc. Bilastine is potent H1 antihistaminic agents used in the therapy of allergic conditions and rhinitis without inducing drowsiness. The current research focused on developing oral thin film of Bilastine for all the allergic conditions. The hydroxypropyl methylcellulose (HPMC) was selected as film former and the physical interaction with Bilastine was confirmed with FTIR. The 3^3 Box-Behnken design was applied in the designing of oral thin film which predicted 17 possible runs in Design of Expert (Version 11). The film former (HPMC E15: X1) plasticizer (PEG 400: X2) and superdisintegrants (CCS: X3) were selected as independent parameters and disintegration time (Y1), folding endurance (Y2) and in-vitro dissolution release (Y3) as dependable parameters in the development of oral thin film. The film was prepared by solvent casting method and evaluated. The optimized batch F10 tested for weight variation, folding endurance (135), disintegration time (12 sec), percentage of dissolution (98.70%) and found stable during accelerated stability studies. The fast-dissolving oral thin film of Bilastine (F10) was developed which showed prompt relief from the allergic conditions.

KEYWORDS: Oral thin film; bilastine; allergic rhinitis; hydroxyl propyl methyl cellulose; box-behnken design

1. INTRODUCTION

Allergic rhinitis (AR) is most common chronic diseases causing inflammation of nasal mucosa. The AR is triggered due to the immunoglobulin E (IgE) reaction after a reaction with allergens. The AR is characterized by frequent sneezing, nasal discharge, and nasal congestion. Moreover, the patients suffering with AR also experiences mild fever, headache, fatigue, cognitive impairment, difficulty in sleep and lack of attention. AR is recognized as most predominant allergic disease affecting the population around 12 to 40 % [1, 2, 3]. The dust particles in nearby surroundings, pollens, spores and animal residue generally responsible for initiating AR [4,5]. The allergens promotes the activation of B cells responsible for inducing hypersensitivity reactions and thereby liberated histamine, leukotrienes, prostaglandins D2, thromboxane A2 and platelet-stimulating factor [6, 7].

Solid orals are still most favored dosage forms in the market. They are superior over others dosage forms in terms of convenience, comfort, economic, ease of handling and easy to manufacture on large scale. Sometimes, solid orals are not convenient for pediatrics, geriatric, psychiatric and patients having dysphagia. The population around 28% have observed difficulty in swallowing of solid orals [8, 9]. Hence, the advancement in solid orals initiated from conventional tablets and capsules-mouth dissolving tablet (MDT)-oral thin film (OTF). The OTF gain tremendous significance for possessing benefits of solid orals along with high accuracy, preventing first-pass metabolism, improving bioavailability of poorly soluble and absorbable drugs, etc. [10, 11].

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1214-1229.

ISSN: 2630-6344

http://dx.doi.org/10.29228/jrp.214

The OFT is a thin transparent film which quickly disintegrates in the oromucosal cavity. OTF is highly acceptable dosage form for pediatric, geriatrics, psychiatric, dysphagia and bed-prone patients. OFT is most acceptable dosage form prepared with film formers such as hydroxypropyl methylcellulose, pullulan and polyvinyl alcohol. OTF also includes plasticizer, flavors, colors, sweeteners, superdisintegrants, etc. [12]. Currently, many film are available in market namely, orally disintegrating film, sublingual film, and buccal film. The ideal OTF is thin, flexible and also provides good stability with better manufacturing support [13].

Bilastine is a second-generation antihistaminic agent possesses high affinity for H1 histamine receptor. Bilastine is recommended for the therapy of seasonal rhinitis (nasal and non-nasal) and urticaria. Bilastine rapidly binds with histamine receptor and thereby prevent the liberation which mimic allergic reactions [14]. Moreover, Bilastine have superiority over other antihistaminic as it is non-sedative agent [15].

The current research work stated the development of novel formulation of Bilastine in the form of oral thin film which has high patient compliance, comfort and can be easily administered by pediatric, geriatric and patients suffering with dysphagia. Moreover, prompt action and high therapeutic efficacy can be achieved with OTF technology. Biocompatible polymer HPMC were utilized as film former along with plasticizer PEG with addition of saliva stimulating agent like citric acid, aspartame as sweetener and mint flavor.

Quality-by-design (QbD) explore the systematic development of a pharmaceutical product involving predefined objectives and comprises of product understanding, control and prompt recognition of risk assessments. The principal elements of QbD involves quality targeted product profile (QTPP), critical quality attributes (CQA), critical material attributes (CMA), critical process parameters (CPP), design space and risk assessments (RA). From the perspectives of OTF, QTPP parameters are dosage form, route of administration, dosage strength whereas, disintegration time, dissolution, content uniformity, folding endurance are considered as CQA [16].

The optimization analysis was performed by response surface methodology using Box-Behnken design. In this model, 3-factors were selected and considered as independent parameters such as concentration of film former (HPMC E15), plasticizer (PEG 400) and superdisintegrants (CCS) respectively, whereas disintegration time, dissolution and folding endurance were dependable parameters. The quadratic model were selected for BBD obtained by Design of expert software (Version 11) [17] .

2. RESULTS AND DISCUSSION

2.1. Organoleptic evaluation

Bilastine is white color powder and don't have any odor. The melting point was determined with melting point apparatus and observed in the range of 199-201^0 C. The LOD value was found to be 0. 34 %.

2.2. Compatibility study

The identification of pure sample of Bilastine was carried out with FTIR spectra. The C-H aliphatic stretching was available in the range of 1355-1485 cm^{-1} and observed at 1456.96 cm^{-1} and 1429.96 cm^{-1}. Whereas, C-N stretching predicted in the range of 1266-1342 cm^{-1} and identified at 1351.24 cm^{-1}, C= O stretching (1200-1275 cm^{-1}) recognized at 1255.10 cm^{-1} and C=H stretching (1250-1310 cm^{-1}) at 1378.85 cm^{-1}. The individual peaks of drug and HPMC was clearly reflected in the spectrum, which indicated that Bilastine is compatible with HPMC.

The formulation ingredients should be compatible with the active ingredients to provide high therapeutic efficacy. The compatibility study was carried out with Bilastine and HPMC by FTIR (ATIR-1S-Affinity, Schimadzu, Japan). The FTIR spectrum was depicted in the Fig. 1- 3 respectively.

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

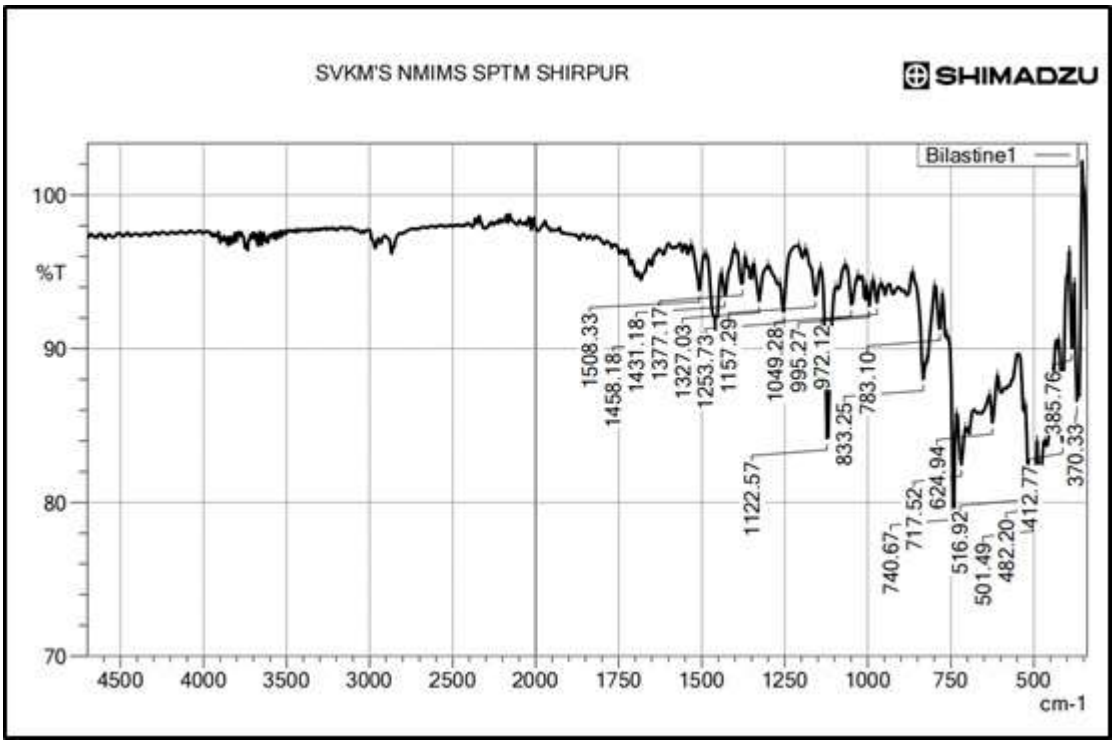

Fig. 1. FTIR Spectra of Bilastine

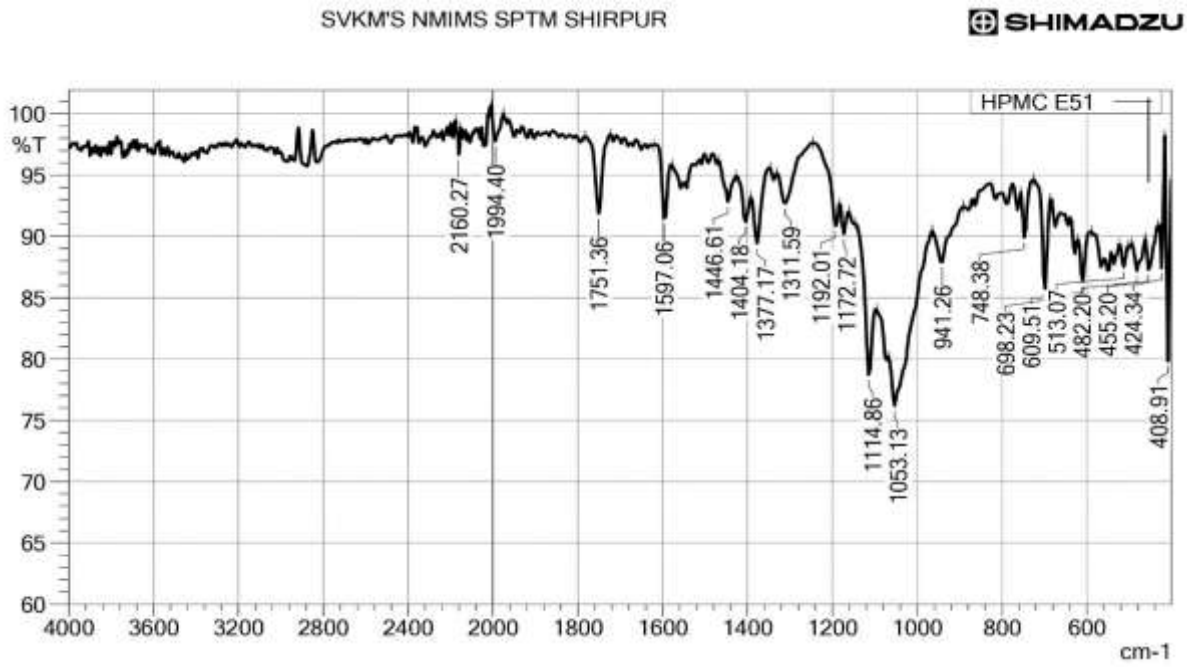

Fig. 2. FTIR Spectra of HPMC.

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

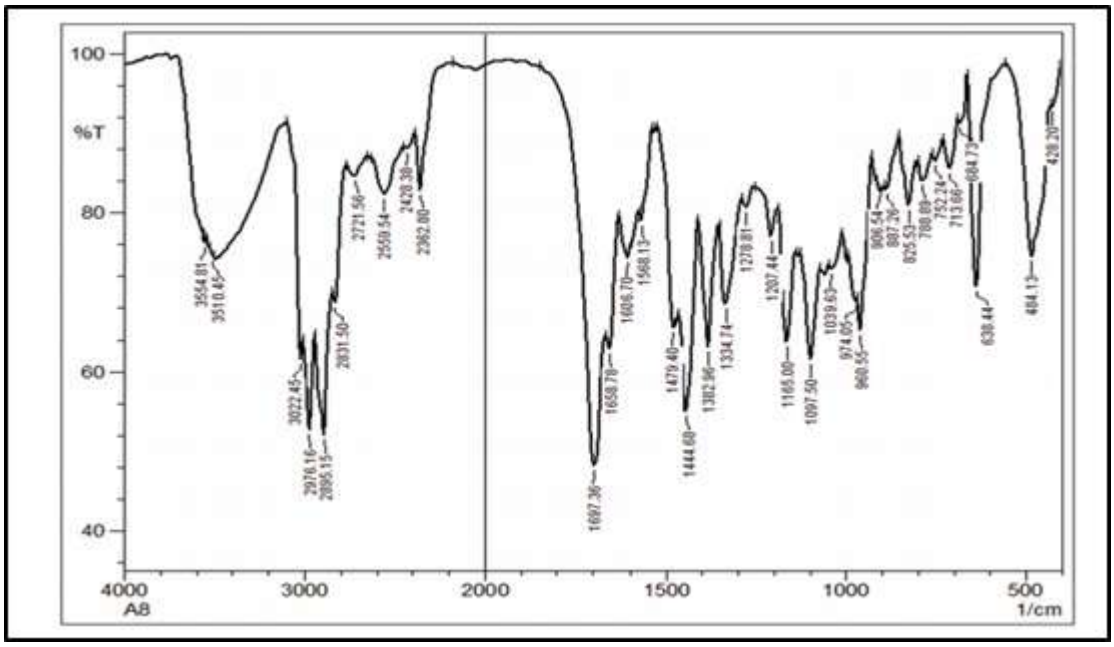

Fig. 3. FTIR of Bilastine and HPMC

2.3. DoE model (Box Behnken design) for drug loaded oral thin film

The optimization software Design of Expert (DoE) of version 11 was applied for the maximum possible runs for the development of oral thin film. The Box-Behnken design was selected for 3 factors (independent factors) predicted 17 possible runs and in actual manner get 13 trial batches after elimination 4 common batches. The DoE of Box-Behnken design was depicted in the **Table 1.**

Table 1: Experimental result of DOE containing different conc. of polymer and plasticizer

		Factor 1	Factor 2	Factor 3	Response 1	Response 2	Response 3
Std	Run	A:HPMC E15	B:PEG 400	C:CCS	Disintegration time	Folding Endurance	Dissolution release
		mg	Mg	mg	Sec	number	%
7	1	300	112.5	8	13	115	98.75
13	2	450	112.5	6	16	110	98.45
6	3	600	112.5	4	19	114	98.75
3	4	300	150	6	16	130	97.69
15	5	450	112.5	6	17	114	98.07
4	6	600	150	6	16	140	98.25
11	7	450	75	8	13	98	98.68
1	8	300	75	6	16	95	97.76
14	9	450	112.5	6	17	105	98.25
16	10	450	112.5	6	16	110	97.7
10	11	450	150	4	20	135	98.15
9	12	450	75	4	19	95	97.9
17	13	450	112.5	6	16	115	97.8
12	14	450	150	8	12	135	98.7
5	15	300	112.5	4	20	110	96.88
2	16	600	75	6	16	95	98.23
8	17	600	112.5	8	13	110	98.5

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

ISSN: 2630-6344
http://dx.doi.org/10.29228/jrp.214

Moreover, ANOVA was also applied for the fit statistics and linear model for all the 3-responses such as disintegration time, folding endurance and in-vitro dissolution studies. The model for all the responses such as disintegration time, folding endurance and dissolution were found to be significant (0.0001, 0.0001 and 0.0241 respectively) identified by the p-value less than 0.05. The ANOVA for the dependable parameters were depicted in the **Table 2, 3 and 4** respectively.

Response 1: Disintegration time

Table 2: ANOVA model for Disintegration time

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	91.25	3	30.42	122.78	< 0.0001	significant
A-HPMC E15	0.1250	1	0.1250	0.5046	0.4900	
B-PEG 400	0.0000	1	0.0000	0.0000	1.0000	
C-CCS	91.13	1	91.13	367.83	< 0.0001	
Residual	3.22	13	0.2477			
Lack of Fit	2.02	9	0.2245	0.7484	0.6715	not significant
Pure Error	1.20	4	0.3000			
Cor Total	94.47	16				

Factor coding is **coded**.

Sum of squares is **Type III - Partial**

The **Model F-value** of 122.78 implies the model is significant. There is only a 0.01% chance that an F-value this large could occur due to noise.

P-values less than 0.0500 indicate model terms are significant. In this case C is a significant model term. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

The **Lack of Fit F-value** of 0.75 implies the Lack of Fit is not significant relative to the pure error. There is a 67.15% chance that a "Lack of Fit F-value" this large could occur due to noise. Non-significant lack of fit is good -- we want the model to fit.

Response 2: Folding Endurance

Table 3: ANOVA model for folding endurance

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	3093.25	3	1031.08	67.60	< 0.0001	significant
A-HPMC E15	10.13	1	10.13	0.6638	0.4299	
B-PEG 400	3081.13	1	3081.13	202.01	< 0.0001	
C-CCS	2.00	1	2.00	0.1311	0.7231	
Residual	198.28	13	15.25			
Lack of Fit	135.48	9	15.05	0.9588	0.5630	not significant
Pure Error	62.80	4	15.70			
Cor Total	3291.53	16				

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

Factor coding is **coded**.
Sum of squares is **Type III - Partial**

The **Model F-value** of 67.60 implies the model is significant. There is only a 0.01% chance that an F-value this large could occur due to noise.

P-values less than 0.0500 indicate model terms are significant. In this case B is a significant model term. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

The **Lack of Fit F-value** of 0.96 implies the Lack of Fit is not significant relative to the pure error. There is a 56.30% chance that a "Lack of Fit F-value" this large could occur due to noise. Non-significant lack of fit is good -- we want the model to fit.

Response 3: Dissolution release

Table 4: ANOVA model for Dissolution release

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	1.97	3	0.6572	4.40	0.0241	significant
A-HPMC E15	0.8778	1	0.8778	5.88	0.0306	
B-PEG 400	0.0060	1	0.0060	0.0405	0.8436	
C-CCS	1.09	1	1.09	7.29	0.0182	
Residual	1.94	13	0.1493			
Lack of Fit	1.56	9	0.1729	1.79	0.3006	not significant
Pure Error	0.3853	4	0.0963			
Cor Total	3.91	16				

Factor coding is **coded**.
Sum of squares is **Type III - Partial**

The **Model F-value** of 4.40 implies the model is significant. There is only a 2.41% chance that an F-value this large could occur due to noise.

P-values less than 0.0500 indicate model terms are significant. In this case A, C are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

The **Lack of Fit F-value** of 1.79 implies the Lack of Fit is not significant relative to the pure error. There is a 30.06% chance that a "Lack of Fit F-value" this large could occur due to noise. Non-significant lack of fit is good -- we want the model to fit.

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

The 3-D response surface graph for disintegration time was obtained after plotting HPMC E15 and PEG 400. This graph illustrates optimum concentration required to prepare good quality film. Whereas, Fig. 4, 5 and 6 illustrated 3-D response surface curves for disintegration time, folding endurance and dissolution respectively when plotted between HPMC E15 and PEG 400.

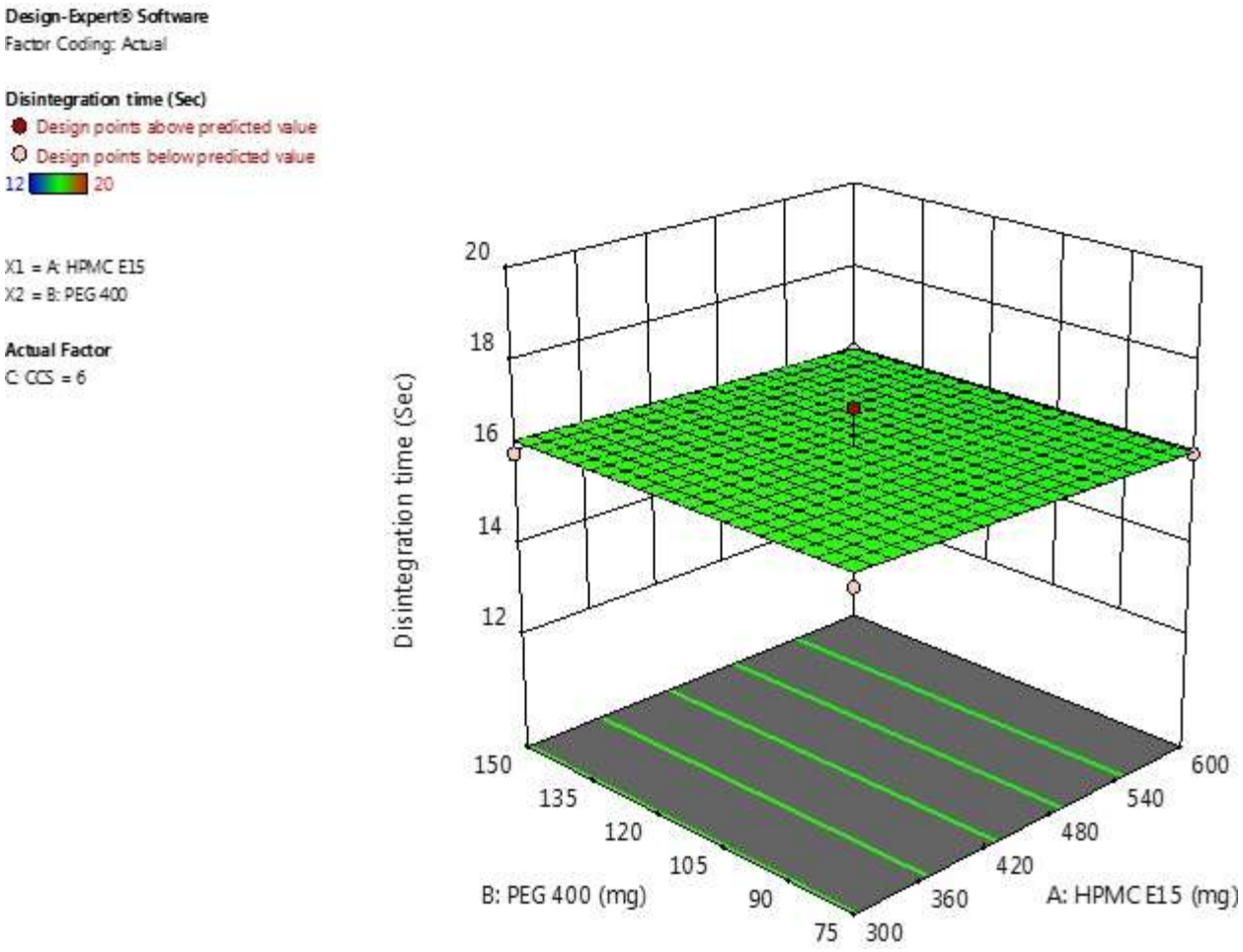

Fig. 4. Response surface plot for Disintegration time.

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

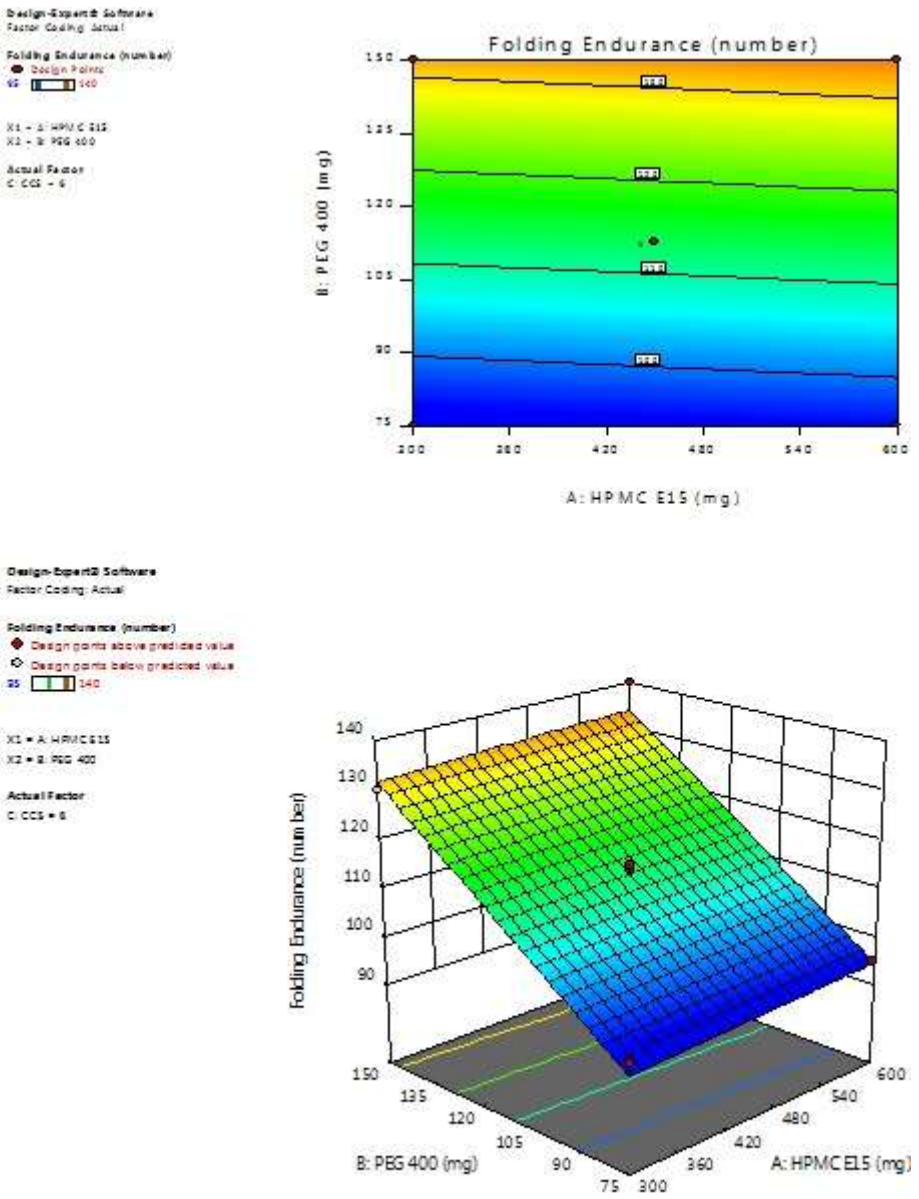

Fig. 5. Response surface plot for folding endurance.

An increase in plasticizer concentration resulted in rise in folding endurance values. Similarly, 3-D response surface graph for dissolution was depicted in Fig. 6. The percentage of drug dissolved rises sharply after increase in concentration of CCS with optimum concentration of HPMC E15 and PEG 400.

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

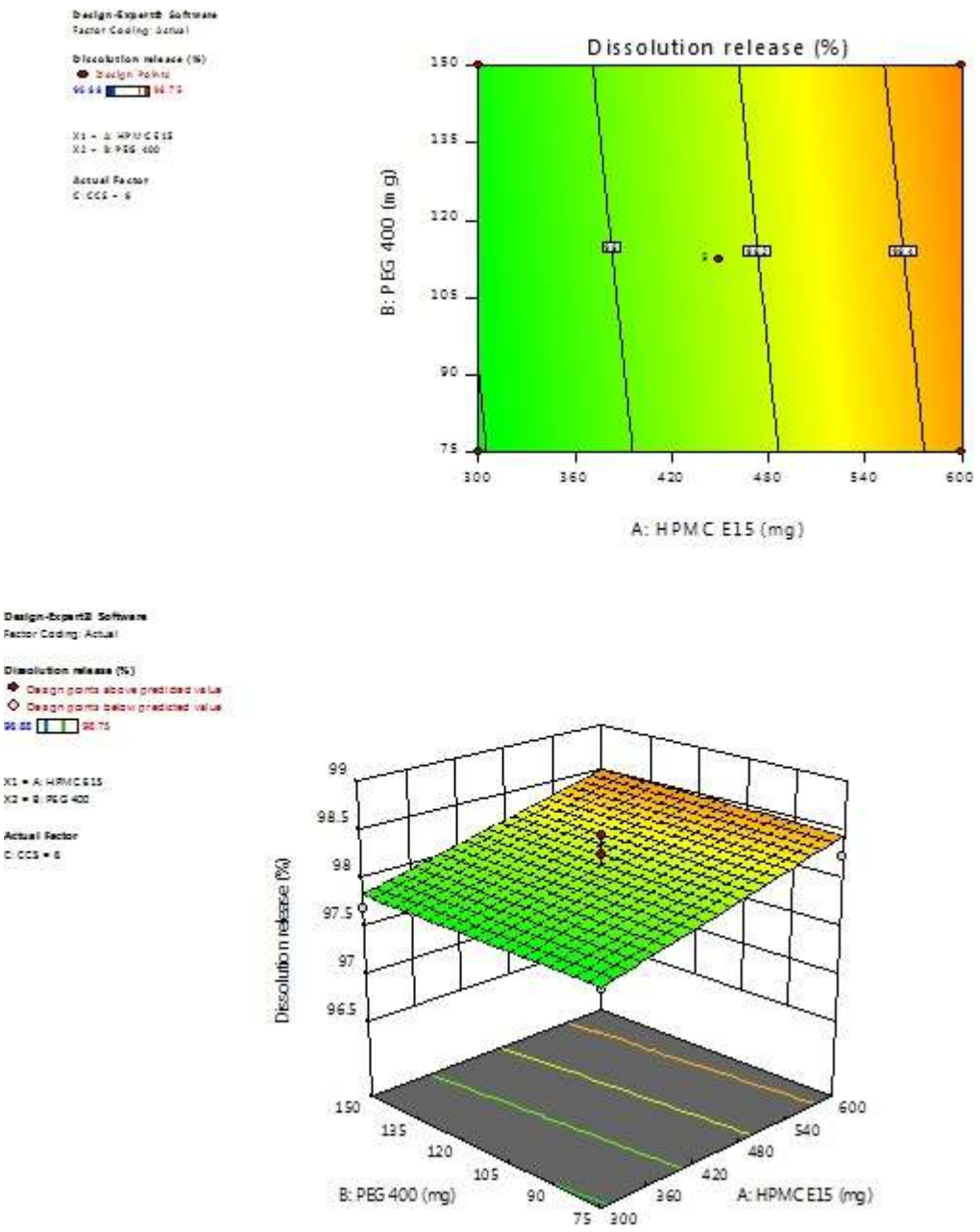

Fig. 6. Response surface plot for Dissolution

2.4. Evaluation of quality of OTF

The developed OTFs were checked for their quality parameters and observed that all the films were of good quality, smooth, transparent and easy to peel off. The image of prepared thin film was depicted in Fig. 7.

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344


Fig. 7. Image of optimized OTF batch F10

2.4.1. Measurement of thickness

The thickness of all prepared films was measured in the range of 55 to 65 µm. An optimum thickness is generally desirable to ensure uniformity. The film should not been too thin (0.035 mm) or thick (0.095 mm) which affects the physical characteristics and disintegration time of the film respectively [18] .

2.4.2. Folding endurance

The flexibility and brittleness of the film was measured by folding endurance. The prepared films were folded repeatedly until it breaks and reading was recorded in the range of 95 to 140. The results of all batches were depicted in **Table 1**.

2.4.3. Determination of pH

The formulated films were dissolved in the 10 ml of the distilled water. The solution was tested for pH and observed in the range of 5.9 to 6.3. These results indicated that the pH of prepared oral thin film were capable of dissolving at oral mucosa.

2.4.4. Disintegration time

The OTFs were placed in the petri dish with 10 ml of artificial saliva fluids and time required to disintegrate completely was noted. The disintegration time for all OTFs were observed in the range of 12 sec to 20 sec. The results of all batches were depicted in **Table 1.**

2.4.5. In-vitro dissolution studies

The in-vitro dissolution studies were performed for all the 13 batches using USP type II paddle apparatus containing 900 ml of the dissolution media. The release of Bilastine from the thin film was very quickest and the complete release was found within 6 min. Among the batches, F10 was quickest released of 98.70 % within 6 min and F8 and F11 were slower release profile with that of F10. During the estimation of dissolution content, sink condition was maintained by replacing the dissolved solution of 5 ml at regular interval with the equal volume of fresh dissolution media in order to prevent not only from saturation of the bulk solution but also retards the dissolution process. Moreover, the prompt release of Bilastine above 98 % indicated that sink condition was maintained during the in-vitro dissolution process. The appropriate quantity of film former, plasticizer and superdisintegrants are desired for the development of oral thin film. The release profile of all the batches were depicted in the Fig. 8 and 9.

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

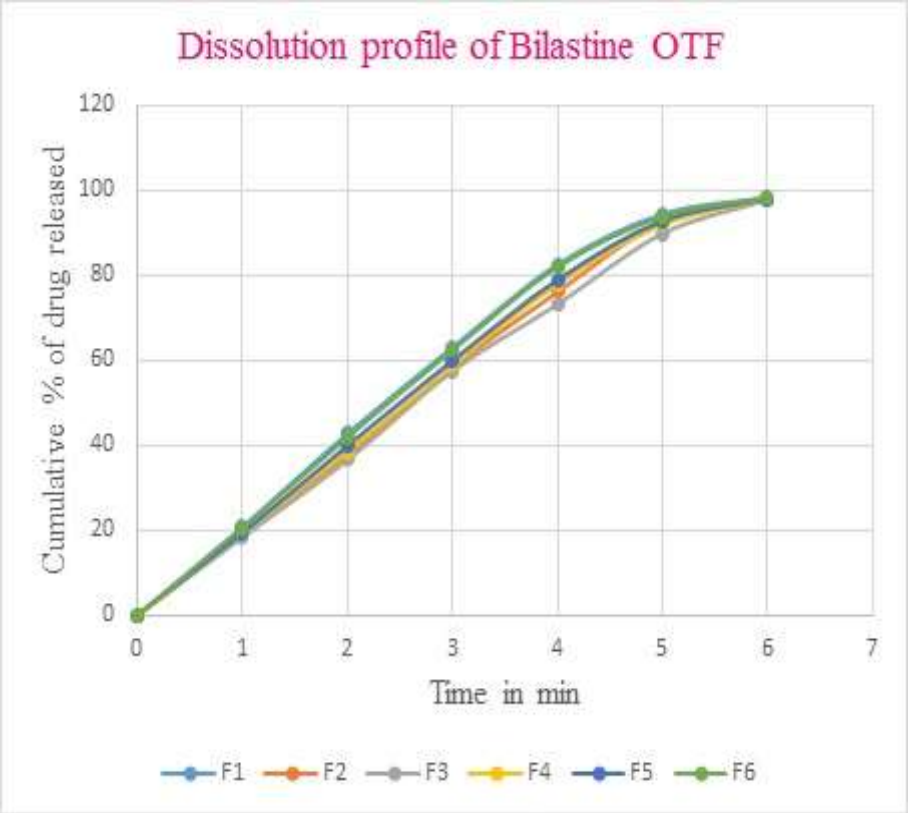

Fig. 8. In-vitro release profile of Batch F1 to F6

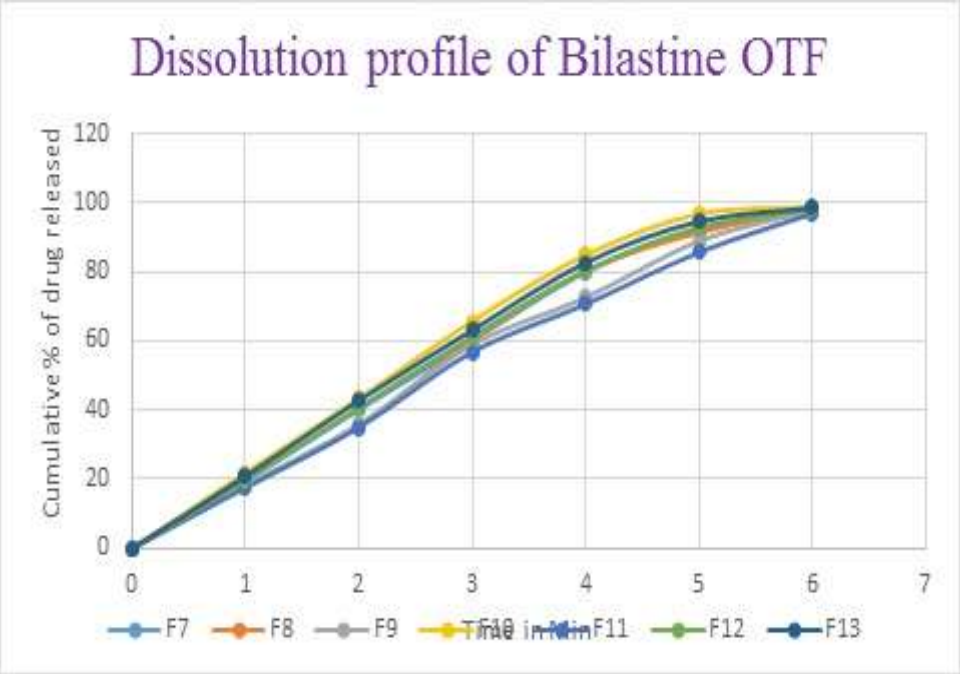

Fig. 9. In-vitro release profile of Batch F7 to F13

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

2.4.6. Content uniformity

One of the major hurdles in the manufacturing of OTF was uniformity in the content. The content uniformity was observed in the range of 96.70 to 98.50 %.

2.5. Stability studies

The optimized batch F10 was subjected under accelerated stability studies at 40^0 C, 75 % relative humidity and samples were withdrawn at regular intervals. The samples were evaluated for disintegration, in-vitro dissolution, folding endurance and content uniformity. The influence of temperature and humidity affects the stability of the OTF due to high percentage of water content. Higher the temperature and humidity greatly affect the quality and stability of the oral thin film. Hence, according to the ICH guidelines, these film were tested at elevated temperature and humidity so as to check the influence on the disintegration, folding endurance and in-vitro dissolution studies which are the critical quality attributes directly related with the patients. Due to high content of water in the OTF, the raised temperature is responsible for evaporation of water, higher humidity resulted in moistening of film causing sticking problem and thereby affect the quality and stability of the film. The result was depicted in the Table 5.

Table 5: Stability studies of an optimized batch F10

Parameters	Initial	After 1 month	After 2 month	After 3 month
Disintegration time	12 Sec	12	11	10
Dissolution	98.70%	98.25%	97.67%	97.22%
Folding endurance	135	130	125	115

All values are calculated with n = 3.

3. CONCLUSION

Recently, oral thin film is gaining tremendous significance for delivery probiotics, therapeutics, proteins, peptides and many nutritional products. OTF is superior over conventional dosage form and hence, widely acceptable. The rise in allergic rhinitis cases is mostly due to the increase in the pollution and sudden environmental changes. The patients suffering from AR will lose patience in severe conditions and hence, requires immediate attention. The medicament delivered through the OTF provides prompt relief from all the conditions associated with the AR. Bilastine OTF was formulated and provides relief from the AR without causing drowsiness.

4. MATERIALS AND METHODS

4.1. Materials

Bilastine was supplied as gift sample from Metrochem API pharmaceuticals, Hyderabad. HPMC E15 was supplied from Nitika Pharmaceuticals, Nagpur. Polyethylene glycol, propylene glycol, citric acid were purchased from Merck chemicals, Mumbai. Aspartame was supplied from Lupin Pharmaceuticals, Aurangabad. All other chemicals utilized were of analytical grade.

4.2. Preformulation studies

Bilastine was characterized for their organoleptic properties such as color and odor. Further, the melting point and loss on drying (LOD) was also estimated with the help of digital melting point apparatus (Lab India) and hot air oven (Alpha Scientific, Bengaluru, India) respectively.

4.3. Interaction study

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

The physical mixture of Bilastine was tested for their compatibility with other formulation ingredients such as HPMC. The mixture was scanned in the range of 400-4000 cm^{-1}. (Shimadzu ATIR) [19] .

4.4. Formulation of OTF of Bilastine

The OTF of Bilastine was developed by solvent casting method [20] . An accurately weighed quantity of film former (HPMC E15) was allowed to dissolve in 10 ml of distilled water with stirring on the magnetic stirrer. The solution was kept aside for about 2 h for swelling characteristics. Moreover, Bilastine was added to 10 ml of distilled water followed by addition of plasticizer (polyethylene glycol) with continuous stirring at 1000 rpm. Then this solution was added slowly in the solution of film former with continuous stirring at 1000 rpm and remaining components until homogenous solution was achieved. The stirring continues up to the removal of any entrapped air bubbles in the solution. Finally, appropriate quantity of citric acid (saliva stimulating agent) and aspartame (sweetener) were added and stirred well. The final solution was caste in the petri plate and kept in an oven at 40-45^0 C for about 12 hrs. After drying, the film was carefully removed and cut into the several number of pieces (2x2 size) [21]F. The formulation components were depicted in **Table 6.**

Table 6 Formulation ingredients for OTF of Bilastine

Batch	Bilastine	HPMC E15	PEG	CCS	Aspartame	Citric acid	Distilled water
F1	5	300	112.5	8	2	1	20
F2	5	450	112.5	6	2	1	20
F3	5	600	112.5	4	2	1	20
F4	5	300	150	6	2	1	20
F5	5	450	112.5	6	2	1	20
F6	5	600	150	6	2	1	20
F7	5	450	75	8	2	1	20
F8	5	300	75	6	2	1	20
F9	5	450	112.5	6	2	1	20
F10	5	450	112.5	6	2	1	20
F11	5	450	150	4	2	1	20
F12	5	450	75	4	2	1	20
F13	5	450	112.5	6	2	1	20
F14	5	450	150	8	2	1	20
F15	5	300	112.5	4	2	1	20
F16	5	600	75	6	2	1	20
F17	5	600	112.5	8	2	1	20

4.5. Optimization by Design of experiments (DoE)

The optimization of OTF of Bilastine was process though Design of experiment (DoE, Version 11 by Stat-Ease) for minimization of any possible errors. In this experiment concentrations of film former HPMC E15 (E15: X1) and plasticizer (PEG: X2) were considered independent parameters, whereas disintegration time (Y1), folding endurance (Y2) and the percentage of dissolution (Y3) were dependable parameters for OTF. The

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

designing study involved utilization of three factors and their two levels (-1, and +1) for the development of OTF of Bilastine was depicted in **Table 7** [22] [23].

Table 7: Optimization of OTF of Bilastine

Factor	Name	Units	Type	Minimum	Maximum	Coded Low	Coded High	Mean	Std. Dev.
A	HPMC E15	mg	Numeric	300.00	600.00	-1 ↔ 300.00	+1 ↔ 600.00	450.00	106.07
B	PEG 400	mg	Numeric	75.00	150.00	-1 ↔ 75.00	+1 ↔ 150.00	112.50	26.52
C	CCS	mg	Numeric	4.00	8.00	-1 ↔ 4.00	+1 ↔ 8.00	6.00	1.41

4.6. Characterization of OTF

4.6.1. Quality of film

The developed film was tested for its quality parameters such as transparency, smoothness and easy to peeling.

4.6.2. Thickness of OTF

The digital calibrated Vernier caliper was used to measure the thickness of the prepared film. The thickness of film was noted from all the corners and at the middle for ensuring uniformity and thereby accuracy in the film [24].

4.6.3. Folding endurance

The flexibility possess by the film was judge with folding endurance. The measurement of folding endurance ensures about strength and brittleness of the film. It was determine by continuous folding of film at the same point until it breaks [25] . The results were carried out in triplicates.

4.6.4. Measurement of pH of OTF

The prepared film was kept in contact with the distilled water and allowed to convert it in solution form inside the petri dish. The solution obtained was subjected to digital pH measurement by electrode (Lab India, Pico model) [26]. The results were carried out in triplicates (n =3).

4.6.5. Disintegration time

The disintegration time of prepared film size (2x2) was placed in the 10 ml of prepared artificial saliva solution. The time required to completely disintegrate was noted in triplicate [27] .

4.6.6. In-vitro dissolution study

The in-vitro dissolution studies were carried out at 37 ±0.5^0 C using USP type II dissolution apparatus (Electolab India, 8 station, Inspire-08). The simulated saliva fluid serves as dissolution media for OTF of Bilastine. The samples of 5 ml were withdrawn at regular interval of 1 min and replaced with 5 ml of salivary fluids to maintain equilibrium. The collected samples were filtered through 0.45 µ filter paper and subjected for scanning under UV visible spectrophotometer at 280 nm [28] . The results were carried out in triplicates (n =3).

4.6.7. Content uniformity

Random selection of OTF film of Bilastine was carried out and further allowed to dissolve in the artificial saliva solution. The solution was further filtered, diluted and characterized with UV visible spectrophotometer at 280 nm [29].

4.7. Stability study

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

The stability study of an optimized OTF of Bilastine was packed in aluminum pouch of required size. This pouch was kept at 40^0 C and 75 % RH for 90 days (Remi India, SC-12 plus). The samples were withdrawn at an interval of one month and tested for disintegration time, folding endurance, in-vitro dissolution and change in thickness [30]. The results were carried out in triplicates (n =3).

Acknowledgement: Authors are thankful to SVKM NMIMS for providing all necessary facilities for the research work.

Author contributions: Concept –A.K.; Y.G; Design – A.K.; Y.G.; Supervision – A.K.; Resources – A.K.; Y.G.; Materials – A.K.; Y.G.; Data Collection and/or Processing – A.K.; Y.G.; Analysis and/or Interpretation – A.K.; Literature Search – A.K.; Y.G; Writing – A.K.; Critical Reviews – A.K.

A.K: Abhishek Kanugo, Y.G: Yash Gandhi.

Conflict of interest statement: The authors declared no conflict of interest.

REFERENCES:

[1]. Gómez RM, Croce VH, Zernotti ME, Muiño JC. Active smoking effect in allergic rhinitis. World Allergy Organ J. 2021;14(2):100504. [CrossRef].

[2]. Rosario Filho NA, Satoris RA, Scala WR. Allergic rhinitis aggravated by air pollutants in Latin America: A systematic review. World Allergy Organ J. 2021;14(8):100574. [CrossRef].

[3]. Choi S, Jung MA, Hwang YH, Pyun BJ, Lee JY, Jung DH, et al. Anti-allergic effects of Asarum heterotropoides on an ovalbumin-induced allergic rhinitis murine model. Biomed Pharmacother. 2021;141:111944. [CrossRef].

[4]. Small P, Keith PK, Kim H. Allergic rhinitis. Allergy, Asthma Clin Immunol. 2018;14(2):1–11. [CrossRef].

[5]. Mengi E, Kara CO, Alptürk U, Topuz B. The effect of face mask usage on the allergic rhinitis symptoms in patients with pollen allergy during the covid-19 pandemic. Am J Otolaryngol. 2022;43(1):103206. [CrossRef].

[6]. Okubo K, Suzuki T, Tanaka A, Aoki H. Efficacy and safety of rupatadine in Japanese patients with seasonal allergic rhinitis: A double-blind, randomized, multicenter, placebo-controlled clinical trial. Allergol Int. 2019;68(2):207–15. [CrossRef].

[7]. Wu TF, Shi WY, Chiu YC, Chan YY. Investigation of the molecular mechanism underlying the inhibitory activities of ethanol extract of Bombyx mori pupa-incubated Cordyceps militaris fruiting bodies toward allergic rhinitis. Biomed Pharmacother. 2021;135:111248. [CrossRef].

[8]. Suryawanshi D, Wavhule P, Shinde U, Kamble M, Amin P. Development, optimization and in-vivo evaluation of cyanocobalamin loaded orodispersible films using hot-melt extrusion technology: A quality by design (QbD) approach. J Drug Deliv Sci Technol. 2021;63:102559. [CrossRef].

[9]. Elbadawi M, Nikjoo D, Gustafsson T, Gaisford S, Basit AW. Pressure-assisted microsyringe 3D printing of oral films based on pullulan and hydroxypropyl methylcellulose. Int J Pharm. 2021;595:120197. [CrossRef].

[10]. Bodini RB, Guimarães J das GL, Monaco-Lourenço CA, Aparecida de Carvalho R. Effect of starch and hydroxypropyl methylcellulose polymers on the properties of orally disintegrating films. J Drug Deliv Sci Technol. 2019;51:403–10. [CrossRef].

[11]. Alaei S, Omidian H. Mucoadhesion and Mechanical Assessment of Oral Films. Eur J Pharm Sci. 2021;159:105727. [CrossRef].

[12]. Takeuchi Y, Nishimatsu T, Tahara K, Takeuchi H. Novel use of insoluble particles as disintegration enhancers for orally disintegrating films. J Drug Deliv Sci Technol. 2019;54:101310. [CrossRef].

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344

[13]. Takeuchi Y, Ikeda N, Tahara K, Takeuchi H. Mechanical characteristics of orally disintegrating films: Comparison of folding endurance and tensile properties. Int J Pharm. 2020;589:119876. [CrossRef].

[14]. Wolthers OD. Bilastine: A new nonsedating oral h1 antihistamine for treatment of allergic rhinoconjunctivitis and urticaria. Biomed Res Int. 2013;2013. [CrossRef].

[15]. Ridolo E, Montagni M, Bonzano L, Incorvaia C, Canonica GW. Bilastine: new insight into antihistamine treatment. Clin Mol Allergy. 2015;13(1). [CrossRef].

[16]. Yu LX, Amidon G, Khan MA, Hoag SW, Polli J, Raju GK, et al. Understanding pharmaceutical quality by design. AAPS J. 2014;16(4):771–83. [CrossRef].

[17]. Zhang L, Mao S. Application of quality by design in the current drug development. Asian J Pharm Sci. 2017;12(1):1–8. [CrossRef].

[18]. Pezik E, Gulsun T, Sahin S, Vural İ. Development and characterization of pullulan-based orally disintegrating films containing amlodipine besylate. Eur J Pharm Sci. 2021;156:105597. [CrossRef].

[19]. Sharma S, Kanugo A, Gaikwad J. Design and development of solid lipid nanoparticles of tazarotene for the treatment of psoriasis and acne: a quality by design approach. Mater. Technol. 2021. [CrossRef]

[20]. Prajapati VD, Chaudhari AM, Gandhi AK, Maheriya P. Pullulan based oral thin film formulation of zolmitriptan: Development and optimization using factorial design. Int J Biol Macromol. 2018;107:2075–85. [CrossRef].

[21]. Han X, Yan J, Ren L, Xue M, Yuan Z, Wang T, et al. Preparation and evaluation of orally disintegrating film containing donepezil for Alzheimer disease. J Drug Deliv Sci Technol. 2019;54:101321. [CrossRef].

[22]. Gupta MS, Kumar TP, Gowda DV, Rosenholm JM. Orodispersible films: Conception to quality by design. Adv Drug Deliv Rev. 2021;178:113983. [CrossRef].

[23]. Al-Mogherah AI, Ibrahim MA, Hassan MA. Optimization and evaluation of venlafaxine hydrochloride fast dissolving oral films. Saudi Pharm J. 2020;28(11):1374–82. [CrossRef].

[24]. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. Int J Pharm Investig. 2013;3(2):67.

[25]. Alhayali A, Vuddanda PR, Velaga S. Silodosin oral films: Development, physico-mechanical properties and in vitro dissolution studies in simulated saliva. J Drug Deliv Sci Technol. 2019;53:101122. [CrossRef].

[26]. Zaki DY, Safwat EM, Nagi SM, Salem HN, Hamdy TM, Moharam LM, et al. A novel dental re-mineralizing blend of hydroxyethyl-cellulose and cellulose nanofibers oral film loaded with nepheline apatite glass: Preparation, characterization and in vitro evaluation of re-mineralizing effect. Carbohydr Polym Technol Appl. 2021;2:100035. [CrossRef].

[27]. Dahmash EZ, Iyire A, Alyami HS. Development of orally dissolving films for pediatric-centric administration of anti-epileptic drug topiramate – A design of experiments (DoE) study. Saudi Pharm J. 2021;29(7):635–47. [CrossRef].

[28]. Zhao Y, Quan P, Fang L. Preparation of an oral thin film containing meclizine hydrochloride: In vitro and in vivo evaluation. Int J Pharm. 2015;496(2):314–22. [CrossRef].

[29]. Bharti K, Mittal P, Mishra B. Formulation and characterization of fast dissolving oral films containing buspirone hydrochloride nanoparticles using design of experiment. J Drug Deliv Sci Technol. 2019;49:420–32. [CrossRef].

How to cite this article: Kanugo A, Yash Gandhi. Formulation optimization and evaluation of oral thin film of bilastine for the treatment of allergic conditions J Res Pharm. 2022; 25(6): 1-XX.

http://dx.doi.org/10.29228/jrp.214
ISSN: 2630-6344